

Fig. 1: Amino acid sequence of the HBsAg a determinant of the different HBV genotypes as compared with the novel variant HDB 11. A representative genome was used as the basis for each genotype and the aa sequence was deduced from the nucleotide sequence A: X70 185; B: D00331; C: X01587; D: X72702, E: X75664; F: X75663; G: FR1 (Stuyver et al.; J. Gen. Virol. 81: 67-74 (2000); Norder et al.: J. Gen. Virol. 73: 3141-3145 (1992))

The amino acid substitutions which differ from the wild-type genotype D, ayw2, HBV are printed in bold type

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Fig. 2 Nucleotide sequence of the S gene of the known HBV ayw2 wild type
 encoding the HBV surface protein (surface antigen, HBsAg), and resulting amino acid sequence in the 3-letter and, especially, 1-letter codes (Coleman et al.; WO 02/079217 A1). Continuous numbering of nucleotides (nt) encoding the surface antigen (excl. pre S1 and pre S2 regions). Continuous numbering of amino acids (aa).

1	ATG AAC ATCACACA TCA GGA TCT CTC GTC TTA CAG GCG GGG TTT TTG	60
20	Met Glu Asn Ile Thr Ser Gly Phe Leu Gly Pro Leu Val Leu Glu Ala Gly Phe Phe	
21	M E N I T S O F L G P L V L Q A G F P	20
61	TTC TCA AGA ATC CTC ACA AT A CCA CAG AGT CTA GACTG TGG TGG TGG ACTCT CTC AAT	120
21	Leu Leu Thr Arg Ile Thr Ser Pro Glu Ser Leu Asp Ser Ttp Tp Thr Ser Leu Asn	40
61	L L T R I L T P D S W W T S L N	
121	TTC TCA GGG GGA ACT ACC GTO GTG CTC GGC CAA AAT TCG CAG ACC TCC AAT CAC	180
21	Phe Leu Gly Thr Val-Gly Glu Asn Ser Glu Ser Pro Thr Ser Asn His	60
41	F L Q T V C L Q N S Q S P T S N H	
181	TCA CCA ACC TCC TGT CCT CCA ACT TGT CCT CGG TGG ATG TGT CTC CGG CGT TTG	240
61	Ser Pro Thr Ser Cys Pro Pro Thr Cys Pro Gly Tyr Arg Thr Met Cys Leu Arg Arg Phe	80
61	S P T S C P Q T C P O Y R W M C L R F	
241	ATC ATC TTC CTC TCA ATC-CTG CTC ATC-CTG CTC ATC-CTG CTC ATC-CTG CTC GACTAT	300
81	Ile Ile Phe Leu Phe Leu Leu Cys Leu Ile Phe Leu Val Leu Leu Asp Tyr	100
81	I I F L P I L L C L I F L V L L D Y	
301	CAA GGT ATG TTG CCG GTT GTG CCT CTA ATT CCA AGG ATCA TCA TCA ACC ACC AGC AGG AGA CCC	360
101	Gln Gly Met Leu Pro Val Cys Pro Phe Ser Thr Thr Ser Thr Gly Pro	120
361	Q G M L C P V S T S T S T S P C P	
121	TGG AGA ACC TCT CCT CAA GGA ACC TCT ATAT CCT CCT CCT TCT TCT TCT ACA	420
421	Cys Arg Thr Cys Thr Thr Pro Ala Glu Gly Thr Ser Met Tyr Pro Ser Cys Cys Thr	140
141	C R T C T P A Q G T S M Y P S C C T	
481	AAA CCT TCG GAT GGA AAC TCC ACC TCT ATT CCT CCA TCA TCT TGG GCT TTC GGA AAA	480
161	Lys Pro Ser Asp Gly Asn Cys Ile Pro Ile Pro Ser Ser Tip Ala Phe Gly Lys	160
161	K P S D G N C T R C I P I P S S W A F G K	
541	TTC CTG TGA GAT TGG ACC CTC TCT TGG CTC ACT TT A CTA GTC CCA TTT GTT	540
181	Phe Leu Ttp Glu Ttp Ala Ser Ala Arg Phe Ser Ttp Leu Ser Leu Val Pro Phe Val	180
541	F. L W B W A S A R F S W L S L L V P F V	
181	CAG TGG TTC CTA GGG CTC TCC CCA ACT GTT TGG CTC TCA ATT ATA TGG ATG ATG TGG TAT	600
201	Gln Ttp Phe Val Gly Leu Ser Pro Thr Val Tp Leu Ser Val His Met Met Tyr	200
201	Q W F V Q L S P T V W L S V I W M M W Y	
661	TGG AGG CCA ACT GTC TACT CTC ACT CTC AGT ACC TTT TCA CGG CTC TTA CGG AAT TTC TTT	660
661	Ttp Gly Pro Ser Leu Tyr Ser Ile Leu Ser Pro Phe Leu Pro Leu Pro Ile Phe Phe	220
661	W G P S L Y S I L S P F L P L L P I F P	
661	TCT CTT TGG TGT ATAC ATT 678	
221	Cys Leu Tp Val Val Tyr Ile 216	

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Fig. 3 Nucleotide sequence of the HBV surface antigen-encoding S gene of the HBV ayw2 wild type (upper row of nt 1 to nt 678) as compared with the nucleotide sequence, which is sequenced from nt 127 to nt 588, of the novel variant HDB 11. (lower row, in which nucleotide differences are printed in bold type and the mutations which do not lead to any amino acid substitution are bracketed)

1	ATG GAG AAC ATC ACA TCA CGA TTC CTA CGG CCC CTC GTC TTA CAG AGC GGC TTT TTC	60
61	TTG TTG ACA AGA ATC CTC ACA ATA CGG CAG AGT CTA GAC TCG TGG TGG ACT TCT CTC AAT	120
121	TTT CTA GGG GGA ACT ACC GTG TGT CTT GGC CAA AAT TCG CAG TCC ACC TCC AAT CAC	180
- 127:	GGG GGA ACT ACC GTG TGT CTT GGC CAA AAT TCG CAG TCC CCA ACC TCC AAT CAC	
181	TCA CCA ACC TCC TGT CCT CCA ACT TGT CCT GGT TAT CGC TGG ATG TGT CTC CGG CGT TTT	240
241	TCA CCA ACC TCC TGT CCT CCA ACT TGT CCT GGT TAT CGC TGG ATG TGT CTC CGG CGT TTT	300
301	ATC ATC TTC CTC CTC ATC CTG CTG CTA TGC CTC ATC TTC TGT TTG GTT CTT CTG GAC TAT	360
361	ATC ATC TTC CTC CTC ATC CTG CTG CTA TGC CTC ATC TTC TGT TTG GCT CTT CTG GAC TAT	420
421	CAA GGT ATG TTG CCC GTT TGT CCT CTA ATT CCA GGA TCA TCA ACC ACC AGC ACG GGA CCC	480
481	CAA GGT ATA TTG CCC GTT TGT CCT CTA ATT CCA GGA (TC) GCA ATC AAC AAC AGG GGACAA	540
541	TGC AAA ACC TGC ACG ACT CCT GCT CAA GGA ACT CCT ATG TAT CCC TCC TGT TGC TGT ACA	600
601	CAA GGT ATG TTG GAG TGG GCC TCA GCC CGT TIC TCT TGG CTC AGT TTA CTA GTG CCA ATT GTT	588
661	TGT CTT TTG GTG GGT TAC ATT	678
	TGG GGG CCA AGT CTG TAC TCC ATC TTG AGT CCC TTT TTA CCG CTG TTA CCA ATT TTCTT	660

Fig. 4 Nucleotide sequence of the S gene of the novel HBV variant HDB 11: nt 127 to nt 588 of the HBV surface antigen-encoding genome. Only the nucleotide differences which lead to a change in the amino acid sequence are printed in bold.

- 127: **G**GG GGA ACT ACC GTG TGT CTT GGC CAA AAT TCG CAG TCC CCA ACC TCC AAT CAC 180
181 TCA CCA **A**CC TCC TGT CCT CCA ACT TGT CCT GGT TAT CGC TGG ATG TGT CTG CGT CGT TTT 240
241 **A**TC ATC TTC CTC ATC CTG CTG CTA TGC CTC ATC TTC TTG TTG GCT CTT CTG GAC TAT 300
301 CAA **G**GT ATA TTG CCC GTT TGT CCT CTA ATT CCA GGA TCT GCA ATC AAC AAC AGG GGACAA 360
361 TGC **A**AA ACC TGC ACG ACT ACT GCT CAC CGG ACC TCT ATG TAT CCC TAC TGT TGC TGT ACC
(AGA, 364-366)
421 AAA CCT TCG GAC **G**GA AAT TGC ACC TGT ATT CCC ATC CCA TCA TCC TGG GCT TTC GGA AAA 480
481 TTC CTA TGG GAG TGG GCC TCA GCC CGT TTCTCC TGG CTC AGT TTA CTA GTT CCC TTT GTT 540
541 CAG TGG TTC GTA **G**GG CTT TCC CCC ACT GTT TGG CTT TCA GGT ATA TGG 588

Fig. 5 S gene nucleotide sequence (nt 127 to 588) and corresponding amino acid sequence (aa 43 to 196) of the novel HBV variant HDB 11 (amino acids which are substituted as compared with the HBV ayw2 wild type are printed in bold and underlined)

127:	GGG GGA ACT ACC GTG TGT CTT GGC CAA AAT TCG CAG TCC CCA ACC TCC AAAT CAC	180
133:	G G T T V C L G Q N S Q S P T S N H	60
181	TCA CCA ACC TCC TGT CCT CCA ACT TGT OCT GGT TAT CGG TGG ATG TGT CTG CGG CGT TTT	240
241	S P T S C P P T C P G Y R W M C L R R F	80
61	ATC ATC TTC CTC TTC ATC CTG CTG CTA TGC CTC ATC TCT TGT TGG GCT CTT CTG GAC TAT	300
81	I I F L P I L L C L I F L L A L D Y	100
301	CAA GGT ATA TTG CCCC GTT TGT CCT CTA ATT CCA GGATCT GCA ATC AAC AAC AGG GGACAA	360
101	Q G I L P V C P L I P G S A I N N R G Q	120
361	TGC AAA ACC TGC ACG ACT ACT GCT CAC CGGA ACC TCT ATG TAT CCCTACT GTG TGT ACC	420
121	C K T C T T A H G T S M Y P Y C C C T	140
	(AGA)	
	(R in a 122)	
421	AAA CCT TCG GAC GGG AAT TGC ACC TGT ATT CCC ATC CCA TCA TCC TGG GCT TTC GGA AAA	480
141	K P S D G N C T C I P I P S S W A P G K	160
481	TTC CTG TGG GAG TGG GCC TCA GCC CGT TCC TGG CTC AGTTTA CTA GTT CCC TTT GTT	540
161	F L W B W A S A R F S W L S L V P F V	180
541	CAG TGG TTC GTG AGG CCT TCC CCC ACT GTT TGG CTT TCA GTT ATA TGG	588
181	Q W F V G L S P T V W L S V I W	-196

The following aa are substituted (x) in the HDB 11 variant as compared with the HBV ayw2 wild type:
 V 96 (A) (not in the region of the a determinant),
 M 103 (I), S 114 (A), T 115 (I), T 116 (N), S 117 (N), T 118 (R), P 120 (Q), T 127 (T), Q 129 (H) and
 S 136 (Y) (all in the region of the a determinant)

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Abb.6 Vergleich der Aminosäure-Sequenzen der a-Determinante (aa 100 bis aa 180) der neuen Variante HDB 11 (untere Reihe) mit dem Wildtyp HBV ayw2 (obere Reihe)

Die folgenden aa sind gegenüber dem Wildtyp HBV ayw2 bei der HDB 11-Variante substituiert (x):
 V 96 (A) (nicht in der Region der a-Determinante),
 M 103 (I), S 114 (A), T 115 (I), T 116 (N), S 117 (N), T 118 (R), P 120 (Q), P 127 (T), Q 129 (H) und
 S 136 (Y) (alle in der Region der a-Determinante)

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